

Amendments to the Specification:

Please add the following new paragraph after the title of the application beginning at page 1, line 1:

Cross-Reference to Related Applications

-- This application is a continuation of U. S. Application 09/563,286, filed May 3, 2000, which is a continuation-in-part of U. S. Application Serial No. 09/428,082, filed October 22, 1999, which claims the benefit of United States Provisional application 60/105,371, filed October 23, 1998, which are incorporated by reference herein. --

Please replace the following paragraphs and table with the following rewritten paragraphs and table:

At page 14, replace lines 22-25, with the following:

Figure 5 shows a synthetic scheme for the preparation of PEGylated peptide 19 (SEQ ID NO: 3) as prepared through intermediates having SEQ ID NOS: 1152 through 1155, respectively.

Figure 6 shows a synthetic scheme for the preparation of PEGylated peptide 20 (SEQ ID NO: 4) as prepared through intermediates having SEQ ID NOS: 1156 and 1157, respectively.

At pageS 51-52, replace Table 12, with the following:

Sequence/structure	SEQ ID NO:
HSDAVFYDNYTR LRKQMAVKKYLN SILN	590
Nle HSDAVFYDNYTR LRKQMAVKKYLN SILN	591
X ₁ X ₁ ' X ₁ " X ₂	592 1142-1151
X ₃ S X ₄ LN	593
NH CH CO KKYX5 NH CH CO X6 (CH2) _m Z (CH2) _n	594
KKYL	595
NSILN	596
KKYL	597
KKYA	598
AVKKYL	599
NSILN	600
KKYV	601
SiLauN	602
KKYLNle	603
NSYLN	604
NSIYN	605

KKYLPPNSILN	606
LauKKYL	607
CapKKYL	608
KYL	NR
KKYNle	609
VKKYL	610
LNSILN	611
YLNSILN	612
KKYLN	613
KKYLNS	614
KKYLNSI	615
KKYLNSIL	616
KKYL	617
KKYDA	618
AVKKYL	619
NSILN	620
KKYV	621
SILauN	622
NSYLN	623
NSIYN	624
KKYLNle	625
KKYLPPNSILN	626
KKYL	627
KKYDA	628
AVKKYL	629
NSILN	630
KKYV	631
SILauN	632

At pages 61-63 replace Table 20, with the following:

Sequence/structure	SEQ ID NO:	Activity
VEPNCDIHVMWEWECFERL	1027	VEGF-antagonist
GERWCDFDGPLTWVCGEES	1084 1141	VEGF-antagonist
GERWCDFDGPLTWVCGEES	1084	VEGF-antagonist
RGWVEICVADDNGMCVTEAQ	1085	VEGF-antagonist
GWDECDVARMWEWECFAGV	1086	VEGF- antagonist
GERWCDFGPRAWVCGWEI	501	VEGF- antagonist
EELWCDFGPRAWVCGYVK	502	VEGF- antagonist
RGWVEICAADDYGRCLTEAQ	1031	VEGF- antagonist
RGWVEICESDVWGRCL	1087	VEGF- antagonist

RGWVEICESDVWGRCL	1088	VEGF- antagonist
GGNECDIARMWEWECFERL	1089	VEGF- antagonist
RGWVEICAADDYGRCL	1090	VEGF-antagonist
CTTHWGFTLC	1028	MMP inhibitor
CLRSGXGC	1091	MMP inhibitor
CXXHWGFXXC	1092	MMP inhibitor
CXPXC	1093	MMP inhibitor
CRRHWGFEFC	1094	MMP inhibitor
STTHWGFTLS	1095	MMP inhibitor
CSLHWGFWWC	1096	CTLA4-mimetic
GFVCSGIFAVGVGRC	125	CTLA4-mimetic
APGVRLGCAVLGRYC	126	CTLA4-mimetic
LLGRMK	105	Antiviral (HBV)
ICVVQDWGHHRCTAGHMANLTSHASAI	127	C3b antagonist
ICVVQDWGHHRCT	128	C3b antagonist
CVVQDWGHHAC	129	C3b antagonist
STGGFDDVYDWARGVSSALTTTLVATR	185	Vinculin-binding
STGGFDDVYDWARRVSSALTTTLVATR	186	Vinculin-binding
SRGVNFSEWLYDMSAAMKEASNVFPSRRSR	187	Vinculin-binding
SSQNWDMEAGVEDLTAAMLGLLSTIHSSSR	188	Vinculin-binding
SSPSLYTQFLVNYESAATRIQDLLIASRPSR	189	Vinculin-binding
SSTGWVDLLGALQRAADATRTSIPPSLQNSR	190	Vinculin-binding
DVYTKKELIECARRVSEK	191	Vinculin-binding
EKGSYYPGSGIAQFHIDYNNVS	192	C4BP-binding
SGIAQFHIDYNNVSSAEGWHVN	193	C4BP-binding
LVTVEKGSYYPGSGIAQFHIDYNNVSSAEGWHVN	194	C4BP-binding
SGIAQFHIDYNNVS	195	C4BP-binding
LLGRMK	279	anti-HBV
ALLGRMKG	280	anti-HBV
LDPAFR	281	anti-HBV
CXXRGDC	322	Inhibition of platelet aggregation
RPLPPLP	323	Src antagonist
PPVPPR	324	Src antagonist
XFXDXWXXLXX	325	Anti-cancer (particularly for sarcomas)
KACRRLFGPVDSEQLSRDCD	326	p16-mimetic
RERWNFDVFTETPLEGDFAW	327	p16-mimetic
KRRQTSMTDFYHSKRRLIFS	328	p16-mimetic
TSMTDFYHSKRRLIFSKRKP	329	p16-mimetic
RRLIF	330	p16-mimetic
KRRQTSATDFYHSKRRLIFSRQIKIWFQNRRMKWKK	331	p16-mimetic
KRRLIFSKRQIKIWFQNRRMKWKK	332	p16-mimetic
Asn Gln Gly Arg His Phe Cys Gly Gly Ala Leu Ile His Ala Arg Phe Val Met Thr Ala Ala Ser Cys Phe Gln	498	CAP37 mimetic/LPS binding

Arg His Phe Cys Gly Gly Ala Leu Ile His Ala Arg Phe Val Met Thr Ala Ala Ser Cys	499	CAP37 mimetic/LPS binding
Gly Thr Arg Cys Gln Val Ala Gly Trp Gly Ser Gln Arg Ser Gly Gly Arg Leu Ser Arg Phe Pro Arg Phe Val Asn Val	500	CAP37 mimetic/LPS binding
WHWRHRIPLQLAAGR	1097	carbohydrate (GD1 alpha) mimetic
LKTPRV	1098	•2GPI Ab binding
NLTTPRV	1099	•2GPI Ab binding
NLTTPRVGGC	1100	•2GPI Ab binding
KDKATF	1101	•2GPI Ab binding
KDKATFGCHD	1102	•2GPI Ab binding
KDKATFGCHDGC	1103	•2GPI Ab binding
TLRVYK	1104	•2GPI Ab binding
ATLRVYKGG	1105	•2GPI Ab binding
CATLRVYKGG	1106	•2GPI Ab binding
INLKALAALAKKIL	1107	Membrane-transporting
GWT	NR	Membrane-transporting
GWTLSAGYLLG	1108	Membrane-transporting
GWTLSAGYLLGKINLKALAALAKKIL	1109	Membrane-transporting
CVHAYRS	1111	Antiproliferative, antiviral
CVHAYRA	1114 1112	Antiproliferative, antiviral
CVHAPRS	1115 1113	Antiproliferative, antiviral
CVHAPRA	1116 1114	Antiproliferative, antiviral
CVHSYRS	1133 1132	Antiproliferative, antiviral
CVHSYRA	1134 1133	Antiproliferative, antiviral
CVHSPRS	1135 1134	Antiproliferative, antiviral
CVHSPRA	1136 1135	Antiproliferative, antiviral
CVHTYRS	1137 1136	Antiproliferative, antiviral
CVHTYRA	1138 1137	Antiproliferative, antiviral
CVHTPRS	1139 1138	Antiproliferative, antiviral
CVHTPRA	1140	Antiproliferative,

	<u>1139</u>	antiviral
HWAWFK	1142 <u>1140</u>	anti-ischemic, growth hormone-liberating

At page 113, replace this paragraph, lines 13-25, with the following:

The Fc portion of the molecule was generated in a PCR reaction with pFc-A3 using the primers

1216-52 AAC ATA AGT ACC TGT AGG ATC G

1798-17 AGA GTA AGT ACC TCC ACC ACC ACC TCC ACC TTT ACC CGG
AGA CAG GGA GAG GCT CTT CTG C

which are SEQ ID NOS: ~~398~~369 and 399, respectively. The oligonucleotides 1798-17 and 1798-18 contain an overlap of 61 nucleotides, allowing the two genes to be fused together in the correct reading frame by combining the above PCR products in a third reaction using the outside primers, 1216-52 and 1798-19.

At page 117, replace this paragraph lines 27-28, with the following:

The nucleotide and amino acid sequences (SEQ ID NOS: ~~—21~~ and ~~—22~~, respectively) of the fusion protein are shown in Figure 16.

At page 118, lines 25-29 and page 119, lines 1-12, replace this paragraph with the following:

Fc-TNF- α inhibitors. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the TNF- α inhibitory peptide was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-EMP fusion strain #3718 (see Example 3) using the sense primer 1216-52 and the antisense primer 2295-89 (SEQ ID NOS: ~~111~~2369 and ~~111~~3398, respectively). The nucleotides encoding the TNF- α inhibitory peptide were provided by the PCR primer 2295-89 shown below:

1216-52 AAC ATA AGT ACC TGT AGG ATC G

2295-89 CCG CGG ATC CAT TAC GGA CGG TGA CCC AGA GAG GTG TTT TTG TAG
TGC GGC AGG AAG TCA CCA CCA CCT CCA CCT TTA CCC

The oligonucleotide 2295-89 overlaps the glycine linker and Fc portion of the template by 22 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

At page 121, lines 26-29 and page 122, lines 1-14, this paragraph with the following:

Fc-IL-1 antagonist. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of an IL-1 antagonist peptide was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-EMP fusion strain #3718 (see Example 3) using the sense primer 1216-52 and the antisense primer 2269-70 (SEQ ID NOS: ~~442~~369 and ~~448~~1116, respectively). The nucleotides encoding the IL-1 antagonist peptide were provided by the PCR primer 2269-70 shown below:

1216-52 AAC ATA AGT ACC TGT AGG ATC G

2269-70 CCG CGG ATC CAT TAC AGC GGC AGA GCG TAC GGC TGC CAG TAA CCC
GGG GTC CAT TCG AAA CCA CCA CCT CCA CCT TTA CCC

The oligonucleotide 2269-70 overlaps the glycine linker and Fc portion of the template by 22 nucleotides, with the PCR resulting in the two genes being fused together in the correct reading frame.

At page 122, replace this paragraph, lines 24-31, with the following:

IL-1 antagonist-Fc. A DNA sequence coding for an IL-1 antagonist peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The template for the PCR reaction was a plasmid containing an unrelated peptide fused via a five glycine linker to Fc. The nucleotides encoding the IL-1 antagonist peptide were provided by the sense PCR primer 2269-69, with primer 1200-54 serving as the antisense primer (SEQ ID NOS: ~~449~~1117 and 407, respectively). The primer sequences are shown below:

At page 124, replace this paragraph, lines 22-28, with the following:

Fc-VEGF Antagonist. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of the VEGF mimetic peptide was constructed using standard PCR technology. The templates for the PCR reaction were the pFc-A3 plasmid and a synthetic VEGF mimetic peptide gene. The synthetic gene was assembled by annealing the following two oligonucleotides primer (SEQ ID NOS: ~~4420~~1118 and ~~4424~~1119, respectively):

At page 124, replace this paragraph, lines 35-36, with the following:

The two oligonucleotides anneal to form the following duplex encoding an amino acid sequence shown below ~~1122~~1120 and 1121):

At page 125, replace these paragraphs, lines 5-11, with the following:

This duplex was amplified in a PCR reaction using 2293-05 and 2293-06 as the sense and antisense primers (SEQ ID NOS: ~~1125~~1124 and ~~1126~~1125).

The Fc portion of the molecule was generated in a PCR reaction with the pFc-A3 plasmid using the primers 2293-03 and 2293-04 as the sense and antisense primers ~~1123~~1122 and ~~1124~~1123), respectively). The full length fusion gene was obtained from a third PCR reaction using the outside primers 2293-03 and 2293-06. These primers are shown below:

At page 126, replace this paragraph, lines 1-7, with the following:

VEGF antagonist -Fc. A DNA sequence coding for a VEGF mimetic peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The templates for the PCR reaction were the pFc-A3 plasmid and the synthetic VEGF mimetic peptide gene described above. The synthetic duplex was amplified in a PCR reaction using 2293-07 and 2293-08 as the sense and antisense primers (SEQ ID NOS. ~~1127~~1126 and ~~1128~~1127, respectively).

At page 126, replace this paragraph, lines 8-12, with the following:

The Fc portion of the molecule was generated in a PCR reaction with the pFc-A3 plasmid using the primers 2293-09 and 2293-10 as the sense and antisense primers (SEQ ID NOS. ~~1129~~1128 and ~~1130~~1129, respectively). The full length fusion gene was obtained from a third PCR reaction using the outside primers 2293-07 and 2293-10. These primers are shown below:

At page 127, replace this paragraph, lines 7-14, with the following:

Fc-MMP inhibitor. A DNA sequence coding for the Fc region of human IgG1 fused in-frame to a monomer of an MMP inhibitory peptide was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-TNF-•

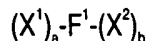
inhibitor fusion strain #4544 (see Example 4) using the sense primer 1216-52 and the antisense primer 2308-67 (SEQ ID NOS: 4112369 and 41311130, respectively). The nucleotides encoding the MMP inhibitor peptide were provided by the PCR primer 2308-67 shown below:

At page 128, replace this paragraph, lines 1-8, with the following:

MMP Inhibitor-Fc. A DNA sequence coding for an MMP inhibitory peptide fused in-frame to the Fc region of human IgG1 was constructed using standard PCR technology. The Fc and 5 glycine linker portion of the molecule was generated in a PCR reaction with DNA from the Fc-TNF- α inhibitor fusion strain #4543 (see Example 4). The nucleotides encoding the MMP inhibitory peptide were provided by the sense PCR primer 2308-66, with primer 1200-54 serving as the antisense primer (SEQ ID NOS: 41321131 and 407, respectively). The primer sequences are shown below:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (currently amended) A composition of matter of the formula



and multimers thereof, wherein:

F¹ is an Fc domain;

X¹ and X² are each independently selected from -(L¹)_c-P¹, -(L¹)_c-P¹-(L²)_d-P², -(L¹)_c-P¹-(L²)_d-P²-(L³)_e-P³, and -(L¹)_c-P¹-(L²)_d-P²-(L³)_e-P³-(L⁴)_f-P⁴

P¹, P², P³, and P⁴ are each independently randomized AGP-3 binding peptide sequences of pharmacologically active peptides;

L¹, L², L³, and L⁴ are each independently linkers; and

a, b, c, d, e, and f are each independently 0 or 1, provided that at least one of a and b is 1 and wherein "peptide" refers to molecules 2 to 40 amino acid and wherein neither X¹ nor X² is a native protein.

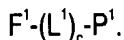
2. (original) The composition of matter of Claim 1 of the formulae



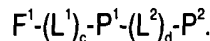
or



3. (original) The composition of matter of Claim 1 of the formula



4. (original) The composition of matter of Claim 1 of the formula



5. (original) The composition of matter of Claim 1 wherein F¹ is an IgG Fc domain.

6. (original) The composition of matter of Claim 1 wherein F¹ is an IgG1 Fc domain.

7. (original) The composition of matter of Claim 1 wherein F¹ comprises the sequence of SEQ ID NO: 2.

8. Claims 8 - 51 (canceled).